Marked-Up Copy of Amended Claim

24. (Amended) A process for producing a polypeptide comprising culturing the host cell of claim 9 under conditions sufficient for the production of said polypeptide from a nucleic acid molecule that encodes said polypeptide, and recovering said polypeptide from the host cell culture.

REMARKS

Applicants have studied the Office Action mailed December 19, 2001. It is respectfully submitted that the application is in condition for allowance. Reconsideration and allowance of the pending claims in view of the above amendments and the following remarks is respectfully requested.

Informalities:

Title

The Examiner objected to the title as being not descriptive.

Applicants have amended the title, as indicated above.

Sequence Rules

The Examiner stated that the application is not fully in compliance with the sequence rules, 37 CFR 1.821-1.825, especially 1.821, part (c), because certain sequences in Figs. 1, 2, and 3 are not accompanied by the required reference to a unique sequence identifier (i.e., SEQ ID NO:).

In response, Applicants submit herewith a substitute Sequence Listing containing the sequences in the Figures, which are required to have SEQ ID NOS (SEQ ID NOS 1-3). The amended drawings submitted herewith are identical to the originally filed drawings except for the insertion of the sequence identifiers. Thus, no new matter is included in any of the amended drawings submitted herewith.

Rejection under 35 USC §101 and §112, 1st paragraph:

The Examiner has rejected claims 4, 8, 9, and 24-29 under 35 U.S.C.§101 and §112, 1st paragraph. In summary, the Examiner has stated that the claimed isolated nucleic acid molecules lack a credible, specific and substantial utility or a well-established utility and, consequently, one skilled in the art would not know how to use the claimed invention.

The Examiner addresses in turn why each of the following asserted utilities are not credible, specific, and/or substantial utilities for the claimed nucleic acid molecules or the polypeptide of SEQ ID NO:2 encoded thereby: 1) to produce a variant or chimeric nucleotide or polypeptide; 2)

to search for drugs as ligands or antagonists; 3) for the production of antibodies; 4) to make hybridization probes and primers to detect nucleic acid molecules that encode the polypeptide of SEQ ID NO:2 and to localize gene expression in tissue samples; 5) in the creation of transgenic animals; 6) to detect polymorphisms in individuals; and 7) for clinical therapy using the polypeptide or ligand.

The Examiner states that, due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide encoded by the claimed polynucleotides such that it can be determined how to use the claimed polynucleotides and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicants respectfully traverse this rejection based on the following remarks.

Contrary to the Examiner's assertions, the claimed isolated nucleic acid molecules, such as SEQ ID NOS:1 and 3, that encode a specified amino acid sequence, SEQ ID NO:2, and methods of making and using such nucleic acid molecules have several uses that meet the requirements of 35 U.S.C.§101 and the first paragraph of 35 U.S.C.§112. These, as well as the accepted state of the art view that such molecules have uses within the commercial marketplace in the drug development cycle, since they encode previously unidentified members of important pharmaceutical targets, establishes the utility of the claimed invention.

The utility requirement of a claimed invention requires that an invention must have a specific, substantial and credible utility. These requirements are defined in broad terms in cases such as *Brenner v. Manson,* 148 USPQ 689 (S. Ct. 1966) and the recently adopted Utility Guidelines from the USPTO.

However, the notion that a recognized valuable addition to even entry points of the drug discovery cycle advances the art sufficient to establish a "usefulness" of a claimed invention should not be ignored. This is supported by previous case law (e.g., *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980)). Accordingly, the present invention, which is drawn to isolated nucleic acid molecules that encode a novel GPCR protein (SEQ ID NO: 2), specifically, a cyclic-nucleotide-gated ion channel protein, has utility in the drug discovery process. The present invention provides sufficient knowledge and information that is beneficial to the public, and provides

sufficient guidance for researchers to use the claimed subject matter to develop disease treatments and/or diagnostics. It is well recognized that GPCR proteins are among the most important target for drug action. The public disclosure of a new member of the GPCR family through the patenting process clearly advances the art and augments the capabilities of biomedical researchers to combat illnesses.

The utility rejection raised by the Examiner also conflicts with the case *Juicy Whip v. Orange Bang* (Fed. Cir. 1999). *Juicy Whip* held that, in order to violate the utility requirement, an invention must be "totally incapable of achieving a useful result." The polypeptides and encoding nucleic acid molecules of the present invention are well known in the art to be valuable drug targets and therefore have readily apparent commercial utilities, such as for screening potential drug compounds, producing antibodies, developing hybridization probes and primers, etc. In addition to the uses disclosed in the specification and discussed herein for the polynucleotides of the present invention, other utilities are readily apparent to one of ordinary skill in the art based on the observed tissue specific expression patterns. Specifically, the proteins/nucleic acid molecules of the present invention are expressed in humans in the brain, including fetal brain, placenta, liver and kidney. Thus, for example, the proteins/nucleic acids of the present invention are commercially useful for developing therapeutic agents for treating pathologies affecting the brain or other nervous tissue, or for use as tissue markers. Therefore, the present invention is not "totally incapable of achieving a useful result." Instead, it is useful.

Contrary to the Examiner's assertions, Applicants have provided sufficient guidance such that undue experimentation would not be required by one of ordinary skill in the art to determine an activity or property of the disclosed polypeptides in order to know how to use the claimed invention and to screen for activity. For example, the specification and figures show that the protein of the present invention has substantial similarity to GPCR 58. The function of such G-protein coupled receptors is to direct signal transduction within a cell. Upon binding of a ligand to the extracellular portion of such a GPCR receptor, a signal is transduced within the cell that results in a change in a biological or physiological property of the cell. The receptors are part of the components of a modular signaling system that connects the state of intracellular second messengers to extracellular inputs. Such a function is quite specific for this family of molecules and differentiates them from other non-G-protein receptors. As such, this function is specific enough to define a use for GPCR proteins and GPCR-encoding nucleic acid molecules in the

drug discovery process, even though such proteins/nucleic acids may not yet be related to a specific disease or pathological process.

Because of the essential roles that GPCR play a role in signal transduction, it is clear that the discovery of GPCR 58 satisfies a need in the art by providing new compositions which are useful towards the prevention, diagnosis, and treatment of such pathologies. Consequently, one of ordinary skill in the art would recognize that novel GPCR, and encoding nucleic acid molecules, have valuable commercial utilities.

Thus, there is overwhelming evidence in the art to support the utility of novel GPCR proteins and encoding nucleic acid molecules, particularly those related to the GPCR subfamily. Not all nucleic acid molecules, and actually a very limited number, of the 3 billion bases that make up the human genome will encode a protein for these and the other disclosed uses. These uses are quite specific for the GPCR subfamily of proteins, even though each member may play a somewhat different role in cellular responses and pathologies. Even though each member may have a somewhat different role in biology and disease, each is a specific composition of matter having substantial, specific and credible uses that the vast majority of other isolated nucleic acid molecules do not possess.

By placing a new member of the GPCR protein family, particularly a GPCR58, into the public domain through the patenting process, the present invention is not only a clear advancement over the prior art (a newly discovered protein/gene) but also enables significant advancement in medicine and further discovery. The Utility requirement cannot be used to contradict the reasons for the patent system, i.e., to encourage early disclosures of inventions so that others can benefit from, improve upon, and further develop such inventions. This is particularly important in medicine, wherein early disclosure of key inventions (such as new GPCR proteins and encoding nucleic acid molecules) is needed to facilitate the early development of new therapies and diagnostics to treat illnesses.

The grant of a patent to the claimed isolated nucleic acid molecule and the resultant disclosure of the nucleic acid and protein sequences to the public will certainly shorten the process for medical researchers to discover other novel uses for the present GPCR-encoding nucleic acids. One example disclosed in the specification is that the present nucleic acid molecules can be used to produce protein targets for identifying agents that bind to the protein targets and modulate protein function. Such agents can be used to precisely define which

biological and pathological processes the protein is involved in. Furthermore, such agents that bind to a protein target and modulate cellular processes such as cell signaling may subsequently be developed and refined for use in mammalian therapeutic applications. All of this later discovery and refinement will be done using the presently claimed material. These uses are clearly commercial and substantial uses that are specific for a very limited number of proteins/nucleic acid molecules.

In addition to serving as targets for developing molecular probes and therapeutic agents, the disclosed uses of the claimed nucleic acid molecules as probes, primers, and chemical intermediates, particularly in biological assays, is sufficient to satisfy the requirements of 35 USC §101 and §112. The claimed invention is directed to nucleic acid sequences, such as SEQ ID NOS:1 and 3, that encode a GPCR protein, specifically, a GPCR 58, with a specified amino acid sequence (SEQ ID NO: 2). Exemplary uses of the nucleic acid sequences are clearly recited in the specification on, for example, pages 34-57. Among the examples, the nucleic acid molecules are useful as hybridization probes for messenger RNA molecules, transcript/cDNA molecules, genomic DNA, and variants thereof. An expression vector comprising the nucleic acid sequences can be made that expresses the GPCR protein. Such uses are specific for the claimed nucleic acid molecules, and the products of such uses will be clearly different (and hence specific for the claimed molecules) than what would be produced using a different nucleic acid molecule for the same purpose.

In view of law and fact, the utility standard interpreted by the USPTO guidelines is too high. The commercial value of previously unidentified members of the GPCR protein family, particularly novel GPCR 58, members of which are well known in the art to be commercially valuable drug targets, should be sufficient to satisfy the utility requirement. Therefore, applicants respectfully request that the Examiner withdraw the rejection.

Rejection under 35 USC §112, 2nd paragraph-indefiniteness:

The Examiner has rejected claim 24 as being indefinite because the specification does not teach how to recombinantly produce a polypeptide from the complementary nucleic acid (as cited in claim 4(d)).

In response, Applicants have amended claim 24, as indicated above.

Conclusions

By way of the amendments above, claim 24 has been amended. As such, claims 4, 8-9, and 24-29 are currently pending.

The amendments to the specification, drawings, and claims add no new subject matter and their entry is respectfully requested.

In view of the above remarks and amendments, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw the objections and rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent at (240) 453-3812 should the Examiner believe a telephone interview would advance prosecution of the application.

Respectfully submitted,
CELERA GENOMICS

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By: _____
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Attachment: Figures with SEQ ID NOs highlighted in red.